AMENDMENTS TO THE CLAIMS

1.-6. (Canceled)

7. (Withdrawn) A method of treating, stabilizing or preventing a lower than desired total body weight or a lower than desired percentage of body fat in a mammal comprising:

selecting a mammal in need of treatment for having a lower than desired total body weight or a lower than desired percentage of body fat; and

administering to the mammal a compound that decreases Shp2 activity.

8. (Withdrawn) The method of Claim 7, wherein said compound decreases Shp2 activity in neurons of said mammal.

9. (Withdrawn) The method of Claim 8, wherein said compound decreases Shp2 activity in neurons of forebrain of said mammal.

10. (Withdrawn) The method of Claim 9, wherein said compound decreases Shp2 activity in neurons of hypothalamus of said mammal.

11. (Withdrawn) The method of Claim 7, wherein said compound decreases a level of Shp2 mRNA or protein, an activity of Shp2, a half-life of Shp2 mRNA or protein, or a binding of Shp2 to a leptin receptor.

12. (Withdrawn) The method of Claim 11, wherein said compound is a Shp2 antagonist.

13. (Canceled)

14. (Withdrawn) A screening method for determining a compound useful for treating, stabilizing, or preventing a lower than desired total body weight or a lower than desired percentage of body fat in a mammal, said method comprising

contacting a cell with said compound; and

measuring Shp2 activity in said cell in the presence and absence of the compound, wherein the compound is determined to treat, stabilize, or prevent a lower than desired total body weight or a lower than desired percentage of body fat if the compound decreases the level of Shp2 activity.

15.-25. (Canceled)

26. (Currently amended) A genetically modified mouse ~~comprising a disrupted Shp2 gene,~~ whose genome comprises a homozygous disruption of the endogenous Shp2 gene in at

least a portion of forebrain cells such that no Shp2 is expressed in said portion of forebrain cells, ~~wherein said genetically modified mouse is homozygous for said disrupted Shp2 gene, and~~ wherein said genetically modified mouse exhibits an increased body weight in comparison to a mouse ~~that does not have a~~ whose genome does not comprise said disrupted Shp2 gene.

27. (Cancelled)

28. (Previously presented) The genetically modified mouse of Claim 26, wherein said mouse has early-onset obesity.

29. (Currently amended) The genetically modified mouse of Claim 26, wherein said mouse has a resistance to leptin in comparison to a wild-type mouse.

30. (Currently amended) The genetically modified mouse of Claim 26, wherein the Shp2 protein level is decreased by 50-70% in ~~the~~ a forebrain lysate of said mouse in comparison to a wild-type mouse.

31. (Currently amended) The genetically modified mouse of Claim 26, wherein triglyceride levels are increased in the serum of said mouse in comparison to a wild-type mouse.

32. (Cancelled)

33. (Cancelled)

34. (Cancelled)

35. (Cancelled)

36. (Cancelled)

37. (Cancelled)

38. (Cancelled)

39. (Cancelled)

40. (Cancelled)

41. (Cancelled)

42. (Cancelled)

43. (Cancelled)

44. (New) The genetically modified mouse of Claim 26, wherein insulin levels are increased in the serum of said mouse in comparison to a wild-type mouse.

45. (New) The genetically modified mouse of Claim 26, wherein the homozygous disruption of the endogenous Shp2 gene comprises a deletion of exon 4.

46. (New) A genetically modified mouse comprising an increased body weight in comparison to a wild-type mouse, wherein at least a portion of the forebrain of said genetically modified mouse has been genetically altered to lack expression of the endogenous Shp2 gene such that no Shp2 is expressed in said portion of the forebrain, and wherein said genetically modified mouse exhibits an increased body weight in comparison to a mouse that expresses the endogenous Shp2 gene in said portion of the forebrain.

47. (New) The genetically modified mouse of Claim 46, wherein said mouse has early-onset obesity.

48. (New) The genetically modified mouse of Claim 46, wherein said mouse has a resistance to leptin in comparison to a wild-type mouse.

49. (New) The genetically modified mouse of Claim 46, wherein the Shp2 protein level is decreased by 50-70% in a forebrain lysate of said mouse in comparison to a wild-type mouse.

50. (New) The genetically modified mouse of Claim 46, wherein triglyceride levels are increased in the serum of said mouse in comparison to a wild-type mouse.

51. (New) The genetically modified mouse of Claim 46, wherein insulin levels are increased in the serum of said mouse in comparison to a wild-type mouse.

52. (New) The genetically modified mouse of Claim 46, wherein the genetic alteration comprises a deletion of exon 4 in said endogenous Shp2 gene.